

## PATENT COOPERATION TREATY

PCT

Rec'd PCT/TO

12 MAY 2005

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>09586</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, Item 5 below.	
International application No. <b>PCT/JP 03/14622</b>	International filing date (day/month/year) <b>18/11/2003</b>	(Earliest) Priority Date (day/month/year) <b>19/11/2002</b>
Applicant  <b>TAKEDA CHEMICAL INDUSTRIES, LTD.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

## 4. With regard to the title.



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

**INDOLE DERIVATIVES AS SOMATOSTATIN AGONISTS OR ANTAGONISTS**

## 5. With regard to the abstract.



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

## 6. The figure of the drawings to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D209/20 C07D401/12 C07D403/12 C07D417/14 C07D495/04  
 C07D401/14 C07D405/12 C07D417/12 C07D405/14 C07D209/42  
 A61K31/405 A61K31/454 A61K31/497 A61P3/10 A61P3/04

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data, BEILSTEIN Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2002/091090 A1 (HAY BRUCE A ET AL) 11 July 2002 (2002-07-11) paragraph [0013] - paragraph [0056] paragraph [0127] - paragraph [0129] paragraph [0221]; example 21 -----	1-27
X	GB 2 351 733 A (MERCK & CO INC) 10 January 2001 (2001-01-10) claims see definition of t=0 for R3 in claims -----	1-27
P,X	HERNANDEZ, FERNANDO ET AL: "A short synthesis of de-"prenyl"-ardeemin" TETRAHEDRON LETTERS, 44(16), 3367-3369 CODEN: TELEAY; ISSN: 0040-4039, 2003, XP004417076 compounds 7 ----- -/--	1-20



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance  
 "E" earlier document but published on or after the international filing date  
 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  
 "O" document referring to an oral disclosure, use, exhibition or other means  
 "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  
 "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  
 "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  
 "&" document member of the same patent family

Date of the actual completion of the international search

3 June 2004

Date of mailing of the international search report

08. 06. 04

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Kollmannsberger, M

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International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/22577 A (NOVARTIS ERFINDE VERWALT GMBH ; NOVARTIS AG (CH); BAIR KENNETH WALTER ()) 21 March 2002 (2002-03-21) claim 16 page 62; examples 194,197	1-20
X	----- MALY, DUSTIN J. ET AL: "Expedient Solid-Phase Synthesis of Fluorogenic Protease Substrates Using the 7-Amino-4-carbamoylmethylcoumarin (ACC) Fluorophore" JOURNAL OF ORGANIC CHEMISTRY , 67(3), 910-915 CODEN: JOCEAH; ISSN: 0022-3263, 2002, XP002271450 example 8S; table 1	1-20
X	----- DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; ESCHERICH, ACHIM ET AL: "Peptide/benzodiazepine hybrids as ligands of CCKA and CCKB receptors" XP002271451 retrieved from STN Database accession no. 2001:846593 compound with RN 404391-74-8 & BIOPOLYMERS , VOLUME DATE 2000-2001, 56(2), 55-76 CODEN: BIPMAA; ISSN: 0006-3525, 2001,	1-20
X	----- WO 01/74844 A (HOFFMANN LA ROCHE) 11 October 2001 (2001-10-11) claim 1 examples 60-62,94-96	1-20
X	----- WO 01/55106 A (KALVINS IVARS ; KAUSS VALERJANS (LV); STARCHENKOV IGOR (LV); TRAPENCIE) 2 August 2001 (2001-08-02) page 24; example 2.21	1-20
X	----- DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; MERGLER, MONIKA ET AL: "Protected peptide p-nitroanilides by solid-phase synthesis" XP002271452 retrieved from STN Database accession no. 2000:113867 compounds with RN 265327-63-7, 265327-64-8, 265327-70-6, 265327-71-7 & LETTERS IN PEPTIDE SCIENCE , 7(1), 1-7 CODEN: LPSCEN; ISSN: 0929-5666, 2000, ----- -/--	1-20

## INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE CHEMABS [Online]  CHEMICAL ABSTRACTS SERVICE, COLUMBUS,  OHIO, US;  BERNHARDT, ANNE ET AL: "The solid-phase  synthesis of side-chain-phosphorylated  peptide-4-nitroanilides"  XP002271453  retrieved from STN  Database accession no. 1997:535830  compounds with RN 150933-27-0, 194670-62-7  &amp; JOURNAL OF PEPTIDE RESEARCH , 50(2),  143-152 CODEN: JPERFA; ISSN: 1397-002X,  1997,</p> <p>-----</p>	1-20
X	<p>VARNAVAS A ET AL: "ANTHRANOYL-ANTHRANILIC  ACID: A TEMPLATE FOR THE DEVELOPMENT OF A  NEW CLASS OF CHOLECYSTOKININ RECEPTOR  LIGANDS"  PHARMAZIE, VEB VERLAG VOLK UND GESUNDHEIT.  BERLIN, DD,  vol. 51, no. 10,  1 October 1996 (1996-10-01), pages  697-700, XP002056854  ISSN: 0031-7144  example 1; table 1</p> <p>-----</p>	1-20
X	<p>MACOR J E ET AL: "The discovery of a  novel and potent benzodiazepine receptor  pharmacophore"  BIOORGANIC &amp; MEDICINAL CHEMISTRY LETTERS,  OXFORD, GB,  vol. 5, no. 20,  19 October 1995 (1995-10-19), pages  2397-2402, XP004135272  ISSN: 0960-894X  example 1N; table 1</p> <p>-----</p>	1-20
X	<p>DATABASE CHEMABS [Online]  CHEMICAL ABSTRACTS SERVICE, COLUMBUS,  OHIO, US;  GRAF, LASZLO ET AL: "Electrostatic  complementarity within the  substrate-binding pocket of trypsin"  XP002271454  retrieved from STN  Database accession no. 1988:566318  compounds with RN 1116883-22-8,  116906-84-4,  &amp; PROCEEDINGS OF THE NATIONAL ACADEMY OF  SCIENCES OF THE UNITED STATES OF AMERICA ,  85(14), 4961-5 CODEN: PNASA6; ISSN:  0027-8424, 1988,</p> <p>-----</p> <p style="text-align: center;">-/--</p>	1-20

## INTERNATIONAL SEARCH REPORT

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE CHEMABS [Online]            CHEMICAL ABSTRACTS SERVICE, COLUMBUS,            OHIO, US;            TANAKA, TAKUMI ET AL: "Human leukocyte            cathepsin G. Subsite mapping with            4-nitroanilides, chemical modification,            and effect of possible cofactors"            XP002271455            retrieved from STN            Database accession no. 1985:162777            compound with RN 95364-17-3            &amp; BIOCHEMISTRY, 24(8), 2040-7 CODEN:            BICHAW; ISSN: 0006-2960, 1985,</p>	1-13
X	<p>GB 2 140 423 A (KIMBERLY CLARK CO)            28 November 1984 (1984-11-28)            page 10; example 16</p>	1-20
X	<p>DATABASE CHEMABS [Online]            CHEMICAL ABSTRACTS SERVICE, COLUMBUS,            OHIO, US;            BABA, YOSHIHIKO ET AL:            "N.alpha.-Acyl-.alpha.-L-amino acid            anilides"            XP002271456            retrieved from STN            Database accession no. 1978:191467            compound with RN 66253-15-4            &amp; JP 52 148032 A2 (SANKYO CO., LTD.,            JAPAN) 8 December 1977 (1977-12-08)</p>	1-20
P,X	<p>DATABASE CHEMABS [Online]            CHEMICAL ABSTRACTS SERVICE, COLUMBUS,            OHIO, US;            TAKAHASHI, TOSHIHIRO ET AL: "Preparation            of N-phenyl-N-(4-piperidiny)amide            derivatives as peripheral analgesics"            XP002271457            retrieved from STN            Database accession no. 2003:796661            compounds with RN 608536-05-6,            608536-06-7, 608536-07-8, 608536-08-9            abstract            &amp; WO 03/082819 A1 (NIPPON CHEMIPHAR            CO.,LTD., JAPAN)            9 October 2003 (2003-10-09)</p>	28
X	<p>EP 0 761 220 A (LILLY CO ELI)            12 March 1997 (1997-03-12)            page 16 structure IV            page 23; example 13            page 24; example 14</p>	28

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/26188 A (CHRISTNER CLAUDIA ; KUELLERTZ GERHARD (DE); MAX PLANCK GESELLSCHAFT (D) 11 May 2000 (2000-05-11) page 11; example 32 -----	28
X	OJIMA I ET AL: "Design, synthesis and sar of RGD peptide hybrids as highly efficient inhibitors of platelet aggregation" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 5, no. 17, 7 September 1995 (1995-09-07), pages 1941-1946, XP004135341 ISSN: 0960-894X example 5; table 1 -----	28

# INTERNATIONAL SEARCH REPORT

International application No.  
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## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 22, 24 and 26 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1-20 (in part); 27 (in part)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.1

Although claims 22, 24 and 26 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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## Continuation of Box I.2

Claims Nos.: 1-20 (in part); 27 (in part)

The claims are so broadly drafted that the initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible. Consequently, the search has been restricted to:

Compounds and pharmaceuticals of structure (I) in which Z is an optionally substituted cyclic group and A is a phenyl ring, i. e. a combination of claims 5 and 10, thus covering all examples. Use claims 21-26 and claim 28 have been searched completely.

Claim 2 is directed to prodrugs of structurally defined compounds. Since from the term "prodrug" without further definition it is not clear which compounds are actually covered by the claims (Art. 6 PCT) the search with respect to prodrugs has been limited to the possibilities mentioned on pages 50/51 of the description.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.



## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 2002091090	A1	11-07-2002	NONE	
GB 2351733	A	10-01-2001	US 6387932 B1	14-05-2002
WO 0222577	A	21-03-2002	AU 8212901 A	26-03-2002
			BR 0113669 A	03-06-2003
			CA 2420899 A1	21-03-2002
			CN 1450991 T	22-10-2003
			CZ 20030573 A3	18-06-2003
			WO 0222577 A2	21-03-2002
			EP 1318980 A2	18-06-2003
			HU 0300880 A2	28-08-2003
			JP 2004509105 T	25-03-2004
			NO 20030867 A	25-02-2003
			SK 2422003 A3	11-09-2003
			US 2004024067 A1	05-02-2004
			US 2003018062 A1	23-01-2003
WO 0174844	A	11-10-2001	AU 5040701 A	15-10-2001
			CA 2402416 A1	11-10-2001
			WO 0174844 A2	11-10-2001
			EP 1272516 A2	08-01-2003
			JP 2003529607 T	07-10-2003
			US 2003229200 A1	11-12-2003
			US 2001056179 A1	27-12-2001
WO 0155106	A	02-08-2001	AU 2867701 A	07-08-2001
			BR 0107893 A	05-11-2002
			CA 2398728 A1	02-08-2001
			EP 1254114 A2	06-11-2002
			WO 0155106 A2	02-08-2001
			JP 2003520850 T	08-07-2003
			US 2003195212 A1	16-10-2003
GB 2140423	A	28-11-1984	AU 2743284 A	01-11-1984
			BE 899539 A1	16-08-1984
			BR 8401996 A	04-12-1984
			DE 3415636 A1	31-10-1984
			DK 201084 A	29-10-1984
			ES 8604691 A1	01-07-1986
			FI 841686 A	29-10-1984
			FR 2545503 A1	09-11-1984
			IT 1182706 B	05-10-1987
			JP 60037997 A	27-02-1985
			NL 8401375 A	16-11-1984
			NO 841653 A	29-10-1984
			SE 8402305 A	29-10-1984
			ZA 8403169 A	28-11-1984
JP 52148032	A2	08-12-1977	JP 1195097 C	12-03-1984
			JP 52148032 A	08-12-1977
			JP 58026745 B	04-06-1983
WO 03082819	A1	09-10-2003	NONE	
EP 0761220	A	12-03-1997	AU 6772996 A	12-03-1997
			CA 2203428 A1	27-02-1997
			EP 0761220 A1	12-03-1997

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0761220	A	WO 9706803 A1	27-02-1997
		US 5773441 A	30-06-1998
WO 0026188	A	11-05-2000	
		AU 1157900 A	22-05-2000
		WO 0026188 A1	11-05-2000